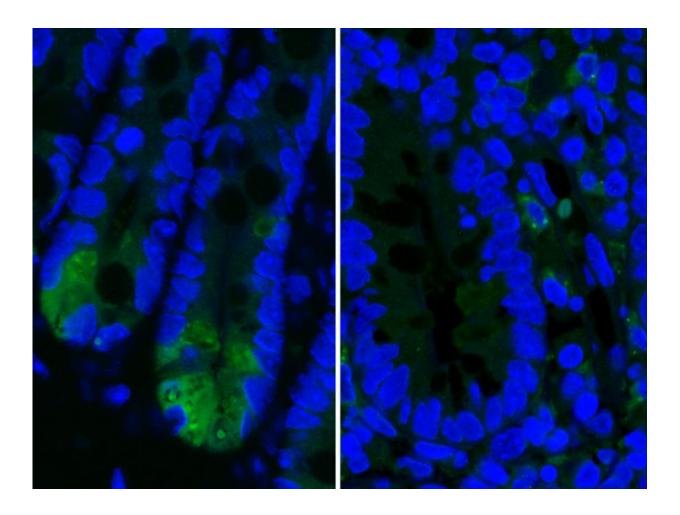


Novel mechanism for Crohn's disease uncovered

April 23 2015



The images show Paneth cells in the small intestine. These cells play an important role in immune defense. In mice with Crohn's-type inflammation, the Paneth cells produce less lysozyme, an important anti-microbial enzyme. Left: Healthy cells producing high levels of lysozyme (light green); right: Damaged Paneth cells producing low levels of lysozyme. Credit: M. Schaubeck / TUM).



Crohn's disease is one of a family of chronic inflammatory bowel diseases (IBD). While it has already been proven to have genetic causes, scientists have now shown that the presence of certain intestinal bacteria also plays a role. A study reported in the *Gut* journal has shown that in mice, bacterial imbalance in the gut can lead to an inflammation similar to Crohn's disease, and this can be transmitted to other animals. With this knowledge, researchers plan to further develop the existing practice of transplanting "healthy" bacteria into patients' intestines and establish this as a conventional treatment for Crohn's disease.

Researchers at Technische Universität München (TUM) have now shown that an unfavorable configuration of bacterial networks in the gut really can cause <u>inflammation</u>. As part of the study, they transplanted the intestinal microbiome from sick animals into the intestines of germ-free mice. These mice developed symptoms specific to Crohn's disease in their small intestine.

"Although we used mice that had an increased genetic disposition towards Crohn's-type inflammation, they did not develop symptoms until we implanted the <u>intestinal bacteria</u> of affected animals," explains Prof. Dirk Haller, TUM Chair of Nutrition and Immunology.

Dysbiosis: a cause of chronic inflammation

One key finding in the study was that chronic IBD is not caused by individual types of bacteria. "It has a lot more to do with the bacterial communities present," says Haller. "It would appear that some combinations of bacteria are 'dysbiotic' - or imbalanced - and their characteristics can now be explained."

The research team was also able to shed more light on the role of Paneth cells - a type of cell found in the epithelial lining of the <u>small intestine</u>. These glandular cells play a role in the gut's immune defense. It has been



known for a while that these cells die in cases of Crohn's disease - but it was not clear whether this cell death triggers the disease or microbial imbalance.

The results of the study indicate that the loss of function in Paneth cells is a result of the inflammation, rather than a cause.

Continued development of an unusual treatment

The research team hope that their findings can help increase the range of treatments available for Crohn's disease. The disease is relatively common: in the developed world, around 40 in 100,000 people will develop Crohn's disease. In Germany, 350,000 people are thought to suffer from the condition.

For many patients, medication only provides short-term relief. "In most cases, the inflammation returns after a time," says Haller. "Stool transplants have already proven effective for a number of intestinal diseases. However, this unusual treatment has yet to deliver conclusive results in patients with Crohn's disease and ulcerative colitis. The findings from our study will help provide a scientific basis for improving this approach - and then it could work."

More information: Dysbiotic gut microbiota causes transmissible Crohn's disease-like ileitis independent of failure in antimicrobial defence; Monika Schaubeck, Thomas Clavel, Jelena Calasan, Ilias Lagkouvardos, Sven Bastiaan Haange, Nico Jehmlich, Martin von Bergen, Aline Dupont, Mathias Hornef, Marijana Basic, André Bleich, Dirk Haller; *Gut* Published Online First; DOI: 10.1136/gutjnl-2015-309333



Provided by Technical University Munich

Citation: Novel mechanism for Crohn's disease uncovered (2015, April 23) retrieved 5 May 2024 from https://medicalxpress.com/news/2015-04-mechanism-crohn-disease-uncovered.html

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